Search Page 33

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NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
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                 frequency
NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
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NEWS  8  Mar 22  TRCTHERMO no longer available
NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                 and USPATFULL
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NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available

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              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'BIOSIS' ENTERED AT 19:24:39 ON 28 APR 2002
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=> s (whey acidic protein) (3a) promoter
L1          106 (WHEY ACIDIC PROTEIN) (3A) PROMOTER

=> s l1 and retrovir?
L2            6 L1 AND RETROVIR?

=> duplicate remove
ENTER L# LIST OR (END):l2
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L3              6 DUPLICATE REMOVE L2 (0 DUPLICATES REMOVED)

=> d 1-6 bib ab

L3   ANSWER 1 OF 6      MEDLINE
Full Text
AN   2002224781      IN-PROCESS
DN   21958721   PubMed ID: 11961665
TI   The murine whey acidic protein promoter directs expression to
     human mammary tumors after retroviral transduction.
AU   Ozturk-Winder Feride; Renner Matthias; Klein Dieter; Muller Mathias;
     Salmons Brian; Gunzburg Walter H
CS   Institute of Virology, University of Veterinary Sciences, A-1210 Vienna,
     Austria.
SO   CANCER GENE THERAPY, (2002 May) 9 (5) 421-31.
     Journal code: 9432230. ISSN: 0929-1903.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   IN-PROCESS; NONINDEXED; Priority Journals
ED   Entered STN: 20020419
     Last Updated on STN: 20020419
AB   The whey acidic protein (WAP) promoter is known to be active in
     pregnant and lactating mammary epithelial cells as well as mammary tumors
     of mice. Here we show that a proximal fragment of the murine WAP promoter,
     including most elements postulated as being responsible for
     mammary-specific regulation, confers mammary-specific expression upon a
     marker gene in transgenic mice even though the distal promoter region,
     known to be important for rat WAP promoter activity, is lacking. The
     relatively small size of this fragment allows its insertion into a murine
     leukemia virus-based retroviral vector in place of the viral promoter.
     Infection of a number of established human mammary and nonmammary cell
     lines with such a retroviral vector revealed that the WAP promoter was
     limited in its activity to mammary tumor cell lines. Expression in
     tumorigenic mammary cells was even more pronounced when these cells were
     introduced into the mammary fat pads of mice. This is the first
     demonstration that the WAP promoter is active in human mammary cells and
     mammary tumor cells in general, and suggests that the extended proximal
     WAP promoter may be useful for directing therapeutic gene expression to
     human mammary tumors. DOI: 10.1038/sj/cgt/7700456

L3   ANSWER 2 OF 6  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN   2001:232581  BIOSIS
DN   PREV200100232581
TI   Impairment of mammary lobular development induced by expression of
     TGFbeta1 under the control of WAP promoter does not suppress tumorigenesis
     in MMTV-infected transgenic mice.
AU   Buggiano, Valeria; Schere-Levy, Carolina; Abe, Keiji; Vanzulli, Silvia;
     Piazzon, Isabel; Smith, Gilbert H.; Kordon, Edith C. (1)
CS   (1) Division Medicina Experimental, Academia Nacional de Medicina, J.A.
```

Pacheco de Melo 3081, 1425, Buenos Aires: edithk@arnet.com.ar Argentina
SO International Journal of Cancer, (15 May, 2001) Vol. 92, No. 4, pp. 568-576. print.
ISSN: 0020-7136.
DT Article
LA English
SL English
AB It has previously been shown that transgenic female mice expressing TGFbeta1 under control of regulatory elements of the whey-acidic protein (WAP) gene were unable to lactate. This was due to the increased apoptosis of the cells committed to the lobular-lactogenic phenotype. Our goal was to determine whether the expression of WAP-TGFbeta1 transgene could inhibit MMTV (mouse mammary tumor virus) tumorigenic activity in the mammary gland. It is well known that the infection with this virus produces focal hyperplastic secretory nodules (HANs) and, some variants can also induce ductal pregnancy-dependent lesions (plaques). In either case, MMTV infection leads ultimately to the appearance of malignant mammary tumors. The results shown herein demonstrate that TGFbeta1 expression in the secretory mammary epithelium does not suppress mammary tumorigenesis in MMTV infected mice. Although MMTV infected WAP-TGFbeta1 transgenic females displayed a strong impairment of lobule-alveolar development, carcinogenesis induced by any of the four MMTV variants used herein proceeded unabated. WAP-TGFbeta1 tumors that showed a strong expression at the WAP promoter, appeared later and grew more slowly than their wild-type counterparts. Transgenic females also had a lower incidence of HANs and plaques. Our study suggests that the epithelial target cells for tumorigenic mutations are probably progenitor cells that are not susceptible to the apoptotic effect of TGFbeta1. Alternatively, their daughters cells that display the secretory phenotype and could be more involved in the formation of premalignant lesions continue to die due to the expression of the transgene.

L3 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1996:229316 BIOSIS
DN PREV199698793445
TI Expression of a truncated Int3 gene in developing secretory mammary epithelium specifically retards lobular differentiation resulting in tumorigenesis.
AU Gallahan, Daniel; Jhappan, Chamelli; Robinson, Gertraud; Hennighausen, Lothar; Sharp, Richard; Kordon, Edith; Callahan, Robert; Merlino, Glenn; Smith, Gilbert H. (1)
CS (1) Build. 10, Room 8B07, Natl. Cancer Inst., NIH, Bethesda, MD 20892-1750 USA
SO Cancer Research, (1996) Vol. 56, No. 8, pp. 1775-1785.
ISSN: 0008-5472.
DT Article
LA English
AB Insertional mutation of the Int3 gene, a member of the Notch gene family, is frequently associated with primary mouse mammary tumors induced by the mouse mammary tumor virus (MMTV). A major consequence of these mutations is the production of a shortened 2.4-kb tumor-specific Int3 RNA transcript that encodes the entire intracellular domain of the Int3 protein. Previous studies have demonstrated that mammary gland development and function was severely impaired in transgenic mice expressing the truncated Int3 gene product from the MMTV viral promoter. Both mammary ductal growth and secretory lobule development were curtailed in these mice. These results were attributed to a gain of function modification of the Int3 gene, which led to a restriction of cell fate selection in the affected mammary epithelial cells. To confirm and extend these findings, truncated Int3 was expressed from the **whey acidic protein** (WAP) **promoter**, the activity of which, unlike that of the MMTV long terminal repeat, is

restricted to the secretory mammary epithelial population. In transgenic mice carrying the WAP/Int3 construct, mammary ductal growth was unaffected in virgin females, but growth and differentiation of secretory lobules during gestation was profoundly inhibited. Coincidental with the block in lobular secretory differentiation, mammary dysplasia and tumorigenesis occurred in all breeding females by 25 weeks of age. In nonbreeding WAP/Int3 females, mammary tumor incidence also reached 100%, but only after 70 weeks. The WAP/Int3 mammary tumors were highly malignant, and most tumor-bearing females, irrespective of breeding history, developed metastatic lung lesions. These results suggest that WAP promoter-targeted Int3 function is associated with mammary secretory cell differentiation and maintenance in this transgenic model. Consistent with the conclusion that WAP-driven truncated Int3 expression influenced only lobular differentiation and not ductal growth and extension during mammary gland development, transplants of WAP/Int3 gland into nontransgenic mammary fat pads produced complete mammary ductal outgrowths in virgin FVB/N mice but failed to develop secretory lobules when the females were impregnated.

L3 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1996:491510 BIOSIS
DN PREV199699213866
TI Hormonal control of transcription from two mammary specific promoters in a rat mammary epithelial cell line.
AU Kilty, Iain C.; Rudland, Philip S.; Barraclough, Roger
CS Dep. Biochemistry, Univ. Liverpool, P.O. Box 147, Liverpool L69 3BX UK
SO Biochemical Society Transactions, (1996) Vol. 24, No. 3, pp. 351S.
Meeting Info.: 658th Meeting of the Biochemical Society Liverpool, England, UK April 16-19, 1996
ISSN: 0300-5127.
DT Conference
LA English

L3 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1996:76329 BIOSIS
DN PREV199698648464
TI Characterization of a protein that binds a negative regulatory element in the mammary-specific **whey acidic protein promoter**.
AU Kolb, Andreas F.; Albang, Richard; Brem, Gottfried; Erfle, Volker; Guenzburg, Walter H.; Salmons, Brian
CS Lehrstuhl Mol. Tierzucht, Ludwig-Maximians-Univ., Munich Germany
SO Biochemical and Biophysical Research Communications, (1995) Vol. 217, No. 3, pp. 1045-1052.
ISSN: 0006-291X.
DT Article
LA English
AB Whey Acidic Protein (WAP) gene expression is restricted to the pregnant and lactating mammary gland. We have recently defined a negative regulatory element (NRE) in the WAP promoter which interacts with a factor (NBF) present in all nonWAP expressing cells (Kolb et al., 1994, J. Cell Biochem. 56:245-261) Here we characterise this factor and show that although it is not related to a number of known transcription factors, including AP-1, NF-1 and SP-1, it may also be involved in controlling the expression from the mouse mammary tumour virus promoter. Three proteins that bind to the WAP-NRE have been identified, one of which is a 53kDa nuclear protein. This protein is present in nonWAP expressing cells, suggesting that it is responsible for limiting WAP expression to the pregnant and lactating mammary gland. This protein has been partially purified and its binding to the WAP-NRE is not appreciably affected by high salt concentrations.

L3 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1993:442985 BIOSIS
DN PREV199345078610
TI Transgenic mouse models of mammary tumorigenesis.
AU Cardiff, Robert D. (1); Muller, William J.
CS (1) Dep. Pathology, Sch. Med., Univ. Calif., Davis, CA 95616 USA
SO Lemoine, N. R. [Editor]; Wright, N. A. [Editor]. Cancer Surveys, (1993) Vol. 16, pp. 97-113. Cancer Surveys; The molecular pathology of cancer. Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive, Plainview, New York 11803, USA.
ISSN: 0261-2429. ISBN: 0-87969-389-4.
DT General Review
LA English

=> d his

(FILE 'HOME' ENTERED AT 19:24:11 ON 28 APR 2002)

FILE 'MEDLINE, BIOSIS' ENTERED AT 19:24:39 ON 28 APR 2002
L1 106 S (WHEY ACIDIC PROTEIN) (3A) PROMOTER
L2 6 S L1 AND RETROVIR?
L3 6 DUPLICATE REMOVE L2 (0 DUPLICATES REMOVED)

=> s l1 and py<1994
L4 22 L1 AND PY<1994

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DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
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PROCESSING COMPLETED FOR L4
L5 15 DUPLICATE REMOVE L4 (7 DUPLICATES REMOVED)

=> d 1-5 bib ab

L5 ANSWER 1 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1994:185983 BIOSIS
DN PREV199497198983
TI Normal and neoplastic growth of mammary glands and circulating levels of prolactin and growth hormone in mouse **whey acidic protein promoter**/human growth hormone (mWAP/hGH) transgenic mice.
AU Nagasawa, Hiroshi (1); Hasegawa, Michiko; Yamamoto, Kazutoshi; Sakamoto, Shinobu; Mori, Takao; Nagumo, Akiko; Tojo, Hideaki
CS (1) Experimental Animal Research Laboratory, Meiji University, Tama-ku, Kawasaki 214 Japan
SO Zoological Science (Tokyo), (1993) Vol. 10, No. 6, pp. 963-970.
ISSN: 0289-0003.
DT Article
LA English
AB Female and male hybrids between SHN females with high mammary tumor potentials and a male transgenic mouse expressing a high human growth hormone (hGH) fusion gene under the control of mouse **whey acidic protein** as a **promoter** were divided into hGH (+) and hGH (-) groups according to serum hGH levels at 50 days of age (111 +- 16 ng/ml and 0.43+-0.05 ng/ml in females and 51+-4 ng/ml and 0.47+-0.05 ng/ml in males, respectively). At both 2 and 4 months of age, female and male hGH (+) mice showed morphometrically a marked stimulation of mammary gland growth. In hGH (+) group, mammary gland contents of DNA and RNA in females and RNA content in males at 2 and 4 months were also significantly higher than in hGH (-) group. Furthermore, in males, thymidylate synthetase and thymidine

kinase activities in the glands were higher in hGH (+) group at 4 month of age. In both females and mates, mammary tumor incidence was enhanced in hGH (+) group. The estrous cycle of hGH (+) females had continued estrus. In both females and males, serum levels of mouse prolactin were higher in hGH (+) group than in hGH (-) group at 4 months. In serum mouse GH levels of both sexes, hGH (+) group was apparently lower and higher than hGH (-) group at 2 and 4 months of age, respectively. The possible role of hGH on normal and neoplastic mammary gland growth was discussed.

L5 ANSWER 2 OF 15 MEDLINE DUPLICATE 1
Full Text
AN 93216538 MEDLINE
DN 93216538 PubMed ID: 8385087
TI Development of a recombinant bovine leukemia virus vector for delivery of a synthetic bovine growth hormone-releasing factor gene into bovine cells.
AU Mehigh C S; Elias V D; Mehigh R J; Helferich W G; Tucker H A
CS Department of Animal Science, Michigan State University, East Lansing 48824.
SO JOURNAL OF ANIMAL SCIENCE, **(1993 Mar)** 71 (3) 687-93.
Journal code: HC7; 8003002. ISSN: 0021-8812.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199305
ED Entered STN: 19930521
Last Updated on STN: 19930521
Entered Medline: 19930506
AB Continuous intravenous infusion of bovine growth hormone-releasing factor (bGRF) increases milk synthesis in dairy cattle by as much as 46%. We have begun to develop a system for delivery and expression of a synthetic bGRF gene in cultured bovine cells using the provirus of the bovine leukemia virus (BLV). The gene encoding synthetic bGRF, constructed from eight overlapping oligonucleotides, was fused to the **whey acidic protein promoter** (WAP) or the mouse mammary tumor virus promoter (MMTV). These plasmids, termed pWAP.GRF and pMMTV.GRF, were able to induce transcription of bGRF upon transfection into Madin-Darby bovine kidney (MDBK) cells and induction with a lactogenic hormonal milieu (prolactin, hydrocortisone, triiodothyronine, insulin) or dexamethasone. When these constructs were cloned into a BLV vector in place of its oncogenic region, and transfected into MDBK cells, bGRF was expressed. Virus particles were prepared from these cultures and used to deliver the bGRF gene by viral infection into fresh MDBK cells. Northern blot analysis of MDBK total RNA revealed a fivefold higher level of expression of bGRF mRNA in transfected cultures than in virally infected cells, and no expression was detected in control cultures. The bGRF peptide was detected in both cell extracts and media samples from transfected cultures but was not detected in cell extracts or media samples from virally infected cells. This provirus construct may prove useful as a delivery system for peptides into cattle.

L5 ANSWER 3 OF 15 MEDLINE
Full Text
AN 93173503 MEDLINE
DN 93173503 PubMed ID: 8437844
TI T1, an immunoglobulin superfamily member, is expressed in H-ras-dependent epithelial tumours of mammary cells.
AU Rossler U; Andres A C; Reichmann E; Schmahl W; Werenskiold A K
CS Department of Cell Chemistry, GSF-Forschungszentrum fur Umwelt und Gesundheit, Neuherberg, Germany.
SO ONCOGENE, **(1993 Mar)** 8 (3) 609-17.
Journal code: ONC; 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
ED Entered STN: 19930402
Last Updated on STN: 19930402
Entered Medline: 19930325
AB T1 is a glycosylated protein in the carcinoembryonic antigen (CEA) family of tumour marker molecules. It was originally identified by virtue of its transient induction after the expression of p21H-ras in NIH3T3 fibroblasts. Here we show that the T1 gene is activated in mammary adenocarcinomas of transgenic mice harbouring an H-ras transgene under the control of the mammary-specific **whey acidic protein** (WAP) **promoter**. By contrast, T1 mRNA was not, or only faintly, detectable in mammary carcinomas of transgenic mice bearing a WAP-myc transgene. Thus, T1 overexpression does not appear to be a general tumour-specific phenomenon. A dependence of T1 gene expression on the action of p21H-ras is suggested by the observation of T1 mRNA in nude mouse tumours generated from H-ras-transformed cultured mammary epithelial cells. Interestingly, activation of the T1 gene is also found during the maturation of the mammary gland (3-4 weeks after birth), whereas it is absent during its terminal differentiation in pregnancy and lactation. This expression pattern suggests a role for the secreted T1 glycoprotein in the phase of epithelial proliferation of the mammary gland. It appears that p21H-ras-induced transformation of mammary epithelial cells mimics the situation occurring in puberty. In both developmental stages the T1 glycoprotein might affect cell interactions of the proliferating epithelial cells with the surrounding stroma. It might thus promote ductal outgrowth in gland maturation as well as invasive growth of p21H-ras-transformed mammary epithelial cells.

L5 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
AN 1993:300369 BIOSIS
DN PREV199396018594
TI Chromosome anomalies in mammary carcinomas from transgenic WAPRAS mice: Comparison with human data.
AU Le Roy, Henri (1); Ricoul, Michelle; Ogata, Hiromitsu; Apiou, Francoise; Dutrillaux, Bernard
CS (1) Lab. de Cytogenetique-Genetique, DSV, DPTE, CEN FAR, B.P. No 6, 92265, Fontenay-aux-Rosés, Cedex France
SO Genes Chromosomes Cancer, (1993) Vol. 6, No. 3, pp. 156-160.
ISSN: 1045-2257.
DT Article
LA English
AB Transgenic WAPRAS mice, obtained by infection of the construct WAP promoter murine gene and the HRAS human protooncogene, develop mammary adenocarcinoma within 1-3 months after pregnancy. A cytogenetic analysis was performed on 17 tumors from 10 mice. Almost all detected anomalies were chromosome gains. The resulting trisomies affected recurrently chromosomes 1, 15, 19, 17, 7, and 12, in decreasing order of involvement. Although in situ hybridization showed that the transgene was integrated in chromosome I, the duplication of this chromosome did not depend on the presence or absence of the transgene. Comparison with human data indicates that the 3 most frequently duplicated chromosomes in WAPRAS mice correspond to the human chromosome segments most frequently duplicated or amplified in breast cancer, i.e., 1q, 8q, and 11q13. None of the chromosome segments often deleted in human tumors were found to be duplicated in the mouse tumors.

L5 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text

AN 1993:387923 BIOSIS
DN PREV199396063223
TI Production and characterization of transgenic mice expressing a hGH fusion gene driven by the **promoter** of mouse **whey acidic protein** (mWAP) putatively specific to mammary gland.
AU Tojo, Hideaki (1); Tanaka, Shin; Matsuzawa, Akio; Takahashi, Michio; Tachi, Chikashi
CS (1) Dep. Appl. Genet., Inst. Anim. Resource Sci., Grad. Sch. Agric. Sci., Univ. Tokyo, Yayoi, Bunkyo-ku, Tokyo 113 Japan
SO Journal of Reproduction and Development, (1993) Vol. 39, No. 2, pp. 145-155.
ISSN: 0916-8818.
DT Article
LA English
AB We have generated 2 transgenic mouse lineages expressing a mWAP/hGH fusion gene where 5' sequence from the mouse whey acidic protein (mWAP) genes is linked to the coding region for human growth hormone (hGH). In the present study, we investigated whether hGH was synthesized in the mammary gland of the transgenic mice and secreted into milk, and whether physiological functions of the transgenic mice were affected by the expression of the transgenes or not. Milk taken from female mice of the transgenic lineages contained from 4.77 +- 0.1 mu-g/ml (n = 4) hGH in average. The hGH was also detected in plasma of the transgenic mice expressing the transgene. The plasma hGH was probably derived from several organs, including submandibular glands, pancreases and tongues as well as mammary glands. The results suggested that expression of the transgenes were probably higher in organs with exocrine functions. In addition, hGH was produced in the brain. Transgenic females derived from one of the founder males showed the sterility accompanied by obesity, insulinemia and hyperglycemia. Histological examination confirmed that the number of azocarmine-positive cells which represent GH secreting-cells in the anterior hypophysis was dramatically reduced in the sterile transgenic females compared to the control mice. The ovary showed signs of pronounced disorders accompanied by failure of follicular growth and by inability of the corpus luteum formation.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.74	24.95

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